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(54) BLOOD FILTER CASCADE

(71) We, PALL CORPORATION, a corporation of the State of New York in the United States of America, whose legal address is Glen Cove, New York, United States of America do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to a blood filter cascade and to a filter unit comprising such a cascade.

There are in general two types of blood filter available on the market for use in human blood transfusions. The most common type is made of wire mesh, or nylon or polyester filament mesh, having a pore size within the range from about 125 to about 140 microns (*Surgical Advances*, Vol. II, No. 6, September, 1951). These filters are referred to as blood strainers. They are very coarse in pore size, because they have a stronge tendency to block quickly if the pore size is any finer.

The other type of blood filter useful in transfusions is a rather thick non woven fibrous mat, usually of polyester fibers, and referred to as a Dacron (Registered Trade Mark) wool filter. This filter is the subject of U.S. patent No. 3,448,041 (inventor R. L. Swank). The filters available commercially have a pore size up to several hundred microns, and are prepared of very fine fibers.

The principle upon which the Swank filter is based is described in that patent at column 3, starting at line 51 and continuing to column 4, line 36. Swank wanted a finely subdivided material having surface characteristics and a size such that it selectively collects the storage-altered components of blood used in blood transfusions. The filter is intended to act as a base to which the adhesive storage-altered platelets and leucocytes adhere. Free passages of the other blood components is supports to be permitted by the filter, which has a large area of adsorbing surface, to achieve a high capacity with a minimum apparatus size. Swank also wanted a material which could be used over long operating periods without collapse or plugging, and without being affected adversely by repeated subjection to heat and chemical sterilization.

The problem of blood strainers is that they do not remove enough of the small finely-divided material, because of their large pore size. On the other hand, the nonwoven fibrous mat filters are at the other extreme. Despite their large pore size, in excess of 100 microns, these filters remove too much material, and also have a very high tendency to block. Large numbers of platelets and white blood cells and bodies of like size in the blood tend to be strained out, leading to rapid blocking, and a compression of the mat under the increased fluid pressure differential thereacross. Both of these effects are undesirable. These results are reported by Egeblad, Osborn, Burns, Hill and Gerbode, *The Journal of Thoracic and Cardiovascular* Surgery, Vol. 63, No. 3, March, 1972, pp. 384-390; and by McNamara, Burran and Suehiro in a paper entitled "Effective Filtration of Banked Blood".

Egeblad et al. report that they had good results using the Dacron wool filter during perfusion for open-heart surgery, where the filter was placed in the line between the cardiotomy reservoir and the main venous line, in which position a large proportion of the circulating blood system bypasses the filter. Such a system requires a much higher rate of flow of blood per unit of time than a blood transfusion system, so that the results obtained repreent results similar to those obtained in blood

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transfusion, but in a shorter time. When placed in the arterial line, so that all blood coming from the oxygenator was filtered, a pressure gradient was built up across the filter, necessitating a switch to another filter hooked up in parallel to the first; and also air was trapped in the filter during initial filling, and was found to be possibly ejected later, directly into the arterial line. The blood reached a very low level of blood platelets within the first ten minutes of use of the filter, and this condition persisted during the entire period of bypass. There was also a drop in white blood cells, and the decrease in both was much more pronounced than usually seen in heart-lung bypass, showing that the filter caught huge amounts of platelets and, to a lesser extent, white cells. The pressure gradient built up across the filter was in part attributed to this mass of cells, and in part to intravascular coagulation with formation of fibrin trapped in the filter. Moreover, the platelets caught on the filter tended to disintegrate subsequently, and the disintegration products entered the filtered blood.

The invention of U.K. Patent No. 1334555 provides a disposable filter element comprising a woven square-weave plastic mesh of polyester monofilaments having a pore size within the range from about 25 to about 50 microns, the filaments being locked in place at their crossing points, and the filaments having a diameter within the range from about 25 to about 50 microns. Such filter elements are capable of removing microemboli from human blood in human blood circulation systems that require circulation of the blood at a high flow rate without removal of normal and desirable blood components. The filter removes not only microemboli but also lipids and debris and gas emboli, and it also has a low resistance at high flow rates and at a high flow capacity, and does not tend to block over long periods of use.

However, for use in blood transfusion, this filter is not fully satisfactory. Blood for use in transfusions has a tendency to contain blood clots, a condition not normally encountered in human blood circulation systems, which utilize the blood of the patent in the circulation system. Blood clots are sticky masses of material, and if large numbers of blood clots are present, the woven square-weave plastic mesh can block very quicky. Moreover, this mesh will pass particles of the size of platelets, and, since platelets in stored blood for transfusion use are non-viable, it is desirable to remove them. If they are removed, however, they must be removed under such circumstances that the red blood cells will still pass through the filter. The white blood cells should pass through the filter, but this is not a prerequisite, since in many conditions where blood transfusions are applied, the patient receiving the transfusion usually has some portion of his normal blood supply present, and this includes platelets and white blood cells.

In accordance with one aspect of the present invention, there is provided a blood filter cascade comprising in combination, three filter sheets, arranged in downstream flow sequence in order of progressively decreasing porosity,

(a) the first filter sheet comprising coarse open netting of filamentary plastics material having a pore size within the range from about 800 to about 4,000 microns;

(b) the second filter sheet comprising an open mesh fabric of plastics monofilaments, having a pore size within the range from 20 to 53 microns; and

(c) the third filter sheet comprising a non-woven fibrous mat having a pore size within the range from 10 to 30 microns.

By this arrangement, there can be provided a blood filter cascade which can be used in blood transfusions with very low risk of blockage, and which is capable of removing not only large particles, such as blood clots, but also small particles, such as platelets, while passing red blood cells and at least a substantial proportion of white blood cells.

The pore size of the first filter sheet may for example be small enough to remove at least a proportion of blood clots which range from 500 to 1000 microns in diameter, and can be coarse enough to do so without being subject to blocking by the blood clots that are strained out. A sheet having a suitably selected pore size of not less than 800 microns can achieve this aim.

The second filter sheet may be an open- or square-weave mesh fabric, and should be adapted to remove microemboli, lipids and debris and gas emboli, in fact virtually all of the particles that pass through the first filter sheet except platelets, white blood cells, red blood cells and other like fine particles.

The third filter sheet should be capable of removing sticky particles of the dimensions of non-viable platelets while permitting most white blood cells to pass through, and also permitting substantially all red blood cells, which have a particle size of approximately 7.5 microns, to pass through.

This combination of filter sheets is referred to as a cascade, because each succeeding filter sheet in the line of flow removes some of the particles passed by the next-preceding filter sheet. The relative proportion of particles removed by the individual

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filter sheets of this filter cascade is distributed among all three filter sheets, so that each filter sheet of the cascade has a low tendency to block over a given blood transfusion to a single patient. For sanitary reasons, blood transfusion filters are not reused, even for the same patient, if a second transfusion is administered at a later time; and since the filters of the invention may be fully disposable, their use resolves the blocking problem common to blood filters which are fine enough to remove small particles such as the adhesive non-viable platelets.

The first filter sheet has an open netting structure. It can be prepared by extruding, casting, or molding plastics into an open-netting having an integral filamentary structure.

The plastics material used should be compatible with blood. Exemplary are polypropylene, polyethylene, polyester, polyamide, and polycarbonate.

One form corresponds to an open square-weave woven filamentary netting, even though it is not manufactured by weaving techniques from filamentary material. An extruded open-mesh plastics filamentary polyprolyene sheet is available commercially under the Registered Trade Mark "Vexar."

Other forms of netting are available which do not correspond to an open square-weave fabric. In these, the filamentary plastics material can be arranged in a manner to define round, elliptical or polygonal openings, which can, for example, be triangular, square, rectangular, pentagonal hexagonal, heptagonal, and octogonal, singly or in pattern combinations. One design, for example, has triangular openings separated by plastics filamentary material and arranged in groups of six to form a hexagonal pattern, and another has triangular openings arranged in groups of two to form a diamond. The shape of the open pores in the netting is in no way critical, but it is important that the pore size is within the range specified above. Pore size is a measurement of the width or diameter across a pore as seen by a particle attempting to pass through it.

The second filter sheet may be a woven open-mesh square-weave fabric which can be made of any plastics monofilament compatible with blood, such as polypropylene, polyethylene, polyester, polyamide, and polycarbonate, and has pore size within the range from 20 to 53 microns. The monofilaments may have a diameter within the range from 20 to 50 microns.

Polyester monofilements are preferred. Most polyester monofilaments available are polyesters of ethylene glycol and terephthalic acid available under the registered Trademark "Dacron". Polyester monofilaments can also be made of other polymers of alkylene glycols and dicarboxylic acids, usually aromatic acids, but also cycloaliphatic and aliphatic acids, for example propylene glycol-1, 2, butylene glycol-2, 3 or -1, 2, or pentylene glycol-1, 2, -2,3 or -1,3, esterified with terephthalic acid or alkyl-substituted terephthalic acids, or adipic or suberic acids, or cyclohexane-1, 4-dicarboxylic acid.

The ethylene glycol-terephthalic acid polyester monofilaments are preferred because of their availablility and low cost. However, polyesters of other glycols and acids can be used.

Exemplary polyester monofilament screen cloths which can be employed as the second filter sheet are made from polyester monofilament 20, 25 and 40 microns in diameter with (a) a mesh opening of 53 microns with 33% open area, (b) a mesh opening of 44 microns with 27% open area, (c) a mesh opening of 37 microns with 23% open area, and (d) a mesh opening of 21 microns with 14.5% open area. Similar screen cloths are available, made of polyamide filaments, polyvinylidene chloride filaments, and polypropylene filaments.

It is also preferred that the monofilaments of the woven square-weave mesh be locked in position at their points of crossing. The locking not only increases strength and rigidity, but it also fixes the pores against change in dimensions in use, which is extremely important.

The third filter sheet is a non-woven fibrous mat. A preferred form of mat is of paper, (which can be of any paper-forming fibrous material, such as cellulose fibers) glass fibres, polyester fibers, polyamide fibers, polyethylene fibers, polypropylene fibers, or polycarbonate fibers. Another type of non-woven mat material is spun bonded plastics sheet, available in polyamide and polyester fibers. Also useful are air-laid or liquid-laid plastics monofilament non-woven mats of fine monofilamentary fibers of any of the above-mentioned plastics materials.

Since the third filter sheet has a pore size within the range from 10 to 30 microns, it is important that the fibers or filamentary material be fine, so as to define pores of the requisite effective dimensions. It is important that there be substantially no pores effectively larger than 30 microns. Since many papers and like nonwoven materials usually have effective pore diameters larger than this, normally within the range from about 200 to about 400 microns, a preferred form of third filter sheet having the requisite pore size

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is obtained by laying down a microporus layer on a coarser substrate having a pore size greater than 30 microns, for instance as described in U.S. patents Nos. 3,238,056 3,247,767 3,353,682 and 3,573,158.

Blood-filter cascades of the invention can be fitted into disposable filter units of any suitable design and configuration. For maximum open area and high flow rate in a confined space. the three filter sheets are preferably assembled in close juxtaposition, with the second and third filter sheets spaced apart, such as when separated by spacers, and all preferably corrugated or convoluted to provide a high surface area to flow.

A spacer between the filter sheets or support material for the sheets will in general be stiffer than the filter sheets, and is preferably fixible, and also preferably of plastics, material so that it can be bonded for instance to the same end cap in a filter unit having an end cap or to a filter bag enclosing the filter sheets cascade. The spacer or support desirably has a pore size at least as large as the first filter sheet, and preferably larger, within the range from 800 to 10,000 microns.

As the spacer or support, any sheet having an uneven surface, such as dimpled, ridged, or quilted, and with large openings therethrough, can be used. Extruded, cast and molded netting are useful, as also are perforated sheets, of polypropylene, polyethylene, polyester, polycarbonate, and polyamide. The surface of the spacer or support is sufficiently uneven so as to provide drainage and prevent blocking of the second and third filter sheets by the spacer or support sheet. A preferred supporting material is Vexar mesh (extruded polypropylene netting).

Th spacer and/or supports can also assist in retaining the filter sheet cascade in a desired shape, such as particularly a corrugated shape. The spacer may be in close juxtaposition to or in contact with the second and third filter sheet of the cascade. However, in general no spacer sheet need precede or follow the first filter sheet of open netting, because of its large pore size.

In another aspect, the invention provides a disposable blood filter unit comprising a blood filter cascade of the invention, and a housing having an inlet port and an outlet port for fluid flow into and out from the housing, the blood filter cascade being disposed in the housing across the line of flow between the inlet and outlet ports so that fluid flow through the housing must pass through the filter cascade.

The housing may comprise two portions bonded together. Preferably the portions are of plastics material and are fused together into an integral structure. Suitably the housing portions, and other parts thereof are of a thermoplastics resin, e.g. polypropylene. Example of such housing are disclosed in U.K. Patent Specification No. 1,372,790.

A suitable configuration of filter unit has the filter sheets in the form of a corrugated cylinder with one of the said ports having a direct fluid flow connection with the interior of the cylinder; the open ends of the cylinder can be closed off by endcaps, limiting access to the filtrate flow line to flow through the filter cascade, the filtrate flow line being in operative connection to at least one of the end caps. This type of construction is shown in U.K. Patent Specification No. 1,334,555. The end caps are preferably of plastics material and can, for example, be of polyester or polypropylene or polycarbonate. The end caps can be bonded to the corrugated filter sheet cascade using a potting compound or an adhesive of conventional type. However, to ensure a leak-tight seal, it is preferred to fuse the end caps to the filter sheet cascade, and for this purpose a polyolefin, such as polyethylene or polypropylene, is preferred as the end cap material. Other plastics materials that can be used as the end caps include polyamides, polycarbonates, and polyester, as well as Teflon polytetrafluoroethylene (Registered Trade Mark "Teflon") and poly trifluorochloroethylene (Registered Trade Mark "Kelef"), but these are more difficult to bond.

Another suitable form of filter unit has the filter sheet cascade and spacer sheets if provided in corrugated form encased in a plastic bag across the line of flow between the inlet and the outlet of the bag, which can, for example, be in the form of line connections such as tubes opening onto opposite sides of the filter sheet cascade. This type is especially useful for attachment to blood transfusion bags, and can be provided with a piercing tube connection for this purpose, if desired.

Filter cascade of the invention can be used in filter units intended for simple blood transfusion where high flow rates are not encountered, as in drip or gravity flow from blood bags, pump-assisted, if desired. The filter unit can accordingly be provided with fittings or line connections suitable to adapt it for in-line connection in blood transfusion systems of any type.

Preferred embodiments of the invention are illustrated in the drawings, in which:

Figure 1 represents a side view, in section, of a filter unit in box form including a three filter sheet cascade, in accordance with the invention;

Figure 2 represents another side view,

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partly in section, of the filter unit of *Figure 1*, showing the side caps on the filter housing portions;

Figure 3 represents a view in detail of a portion in section shown in *Figure 1* of the filter sheet cascade of the invention;

Figure 4 represents an isometric view of filter unit in bag form and comprising a three filter sheet cascade in accordance with the invention;

Figure 5 represents a longitudinal section of the filter unit of *Figure 4*, taken along the line 5-5 and looking in the direction of the arrows; and

Figure 6 represents a cross-section of the filter unit of *Figure 4*, taken along the line 6-6, and looking in the direction of the arrows.

The filter unit of *Figures 1 to 3* is composed of a housing 1 having first and second portions 2 and 3 defining a fluid chamber 4 therewithin. A fluid port 5 opens into the centre of housing channel portion 2, and a fluid port 6 is at the base of housing portion 3. It will be seen that these ports are coaxial. The port 5 serves as a fluid inlet, and the port 6 as a fluid outlet, and flow is only in the direction from port 5 to port 6, because of the arrangement of the three filter sheets in the cascade, as will be seen.

The inlet port 5 is housed in a spiked tube 7 which is designed to pierce a blood bag stopper for use in blood transfusion. Housing portion 2 has an internal projection or rib 8, extending from one side 9 to the other side 10, and housing portion 3 has a similar internal projection 11 extending from one side 12 to the other side 13. These serve as supports extending across the corrugations of a filter sheet cascade and spacer composite 40.

Each housing portion 2 and 3 is generally channel-shaped, with opposed sides 9 and 10 extending outwardly from the base of portion 2, and opposed sides 12 and 13 extending outwardly from the base of portion 3. The housing portions 2 and 3 are each provided with fluid flow ports or channels 14. Portion 2 (see Fig. 2) has on each side a locating flange 15, and portion 3 has on each side two locating flanges 16, defining a channel 17 therebetween into which a flange 15 fits. These flanges locate the portions 2, 3 on assembly. Sides 12, 13 at their ends abut sides 9, 10, and are fused thereto, so that the housing portions are bonded together as one piece. A pair of projecting members 20, 21 on portion 3 extend parallel to and internally of sides 12, 13 all the way to the internal wall of housing portion 2.

The filter sheet cascade and spacer composite 40 (to be described later) at each end or side 22, 23 projects into the sockets 24, 25 defined by sides 12, 13 and members 20, 21, and where the five sheet-composite curves around the tips of members 20, 21, it is held tightly at 26, 27 against the internal wall of portion 2 and is bonded thereto.

The bond is produced by fused integration of the members 20, 21 to the housing portion 2 through the open pores of the three filter sheets 41, 42, 43 and the two spacers or supports 44, 45, forming a fluid-tight seal at 26, 27 all along those sides of the composite, and bonding all five sheets together at those points. Such a bond can be obtained, for example, by ultrasonic welding, by solvent softening, or by heat fusion.

The filter sheet cascade and spacer composite 40, best seen in *Figure 3*, is composed of a first coarse filter sheet 41 of extruded polyproplylene netting (Vexar), pore size about 1500 microns. The two spacers or supports 44, 45 are also made of extruded polypropylene netting (Vexar), of the same pore size, about 1500 microns. The second filter sheet 42 is made of open-mesh square-weave polyester monofilament fabric having a pore opening of 40 microns a monofilament diameter of 40 and 27% open area. The weft monofilaments and the warp monofilaments are locked together by heat setting at their points of crossing defining fixed 40-micron pores at their interstices. The third filter sheet 43 is a microporous filter material composed of paper with a microporous layer of resin-bonded ceramic fibers thereon, prepared following the procedure of U.S. patent No. 3,246,767, issued April 19, 1966, and having a pore size of 15 microns.

The three filter sheets 41, 42, 43 of the filter cascade are in corrugated form, for an increased surface area in the limited space of fluid chamber 4, and the tips of the corrugations abut and are held in place by the projecting sections 8 and 11 of the housing portions 2 and 3. The edges 32,33 of the filter sheet cascade run right to the ends of the sides 12 and 13.

The housing channel portions 2 and 3 are open at their sides and, as best seen in *Figure 2*, define openings 28, 29 leading into the fluid chamber 4 of the housing 1. The openings are closed off by side caps 30, 31 which are bonded to the housing portions 2 and 3 and also to the edges 32 and 33 of the filter sheet cascade and spacer composite 40, extending along the openings from end to end between the mating sections 9, 10, 12 and 13 of the housing portions. This closes off the other two side edges of the filter sheet cascade to fluid flow, and restricts flow between the two portions 34, 35 of fluid chamber

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4 in the housing via the pores in each of the filter sheets in the filter sheet cascade and spacer composite 40. Thus, all flow between fluid ports 5 and 6 of housing 1 must pass through each of the three filter sheets in the direction 41, 42, 43, as is evident from *Figure 3*.

The assembly of the box filter unit of *Figures 1 to 3* is as follows. It will be seen on reference to *Figure 1* that the side sections 9, 10, 12 and 13 of each housing portion 2, 3 have a special construction which ensures a fluid-tight seal between the housing portions when they are bonded together. The opposed sides 9, 10 of housing portion 2 meet and abut like sides 12, 13 of the other housing portion 3. Portion 2 has on each side a-locating flange 15, and portion 3 has on each side two-locating flanges 16, receiving flange 15 therebetween to ensure that the portions fit snugly together in the correct position to hold the filter sheet cascade and spacer composite 40 in place.

The respective pairs of sides 9, 10, 12 and 13 each have a combined length slightly longer before they are bonded together than after. When portions 2 and 3 are fitted together, the sides 9, 10 are readily fused to sides 12, 13, respectively, to produce an integral one-piece structure at the seal 36, *Figure 1*. Internally of the sides 12, 13 in housing portion 3 are the projecting members 20, 21 which extend all the way to the interior wall at 26, 27 of the housing portion 2.

In assembly, the ends or sides 22, 23 of the corrugated filter sheet cascade and spacer composite 40 are folded around the projecting members 20, 21 of housing portion 3 into the sockets 24, 25 between sides 12 13 and the projecting members 20 21, where they are held securely. Housing portion 2 is then fitted over the portion 3, and pressed down smartly against the filter sheet cascade and spacer composite pinching the five sheets at 26, 27 against the tips of projecting members 20, 21, and holding the five sheets firmly in place by the tight engagement between the inner wall of the housing portion 2 and the ends of the members 20, 21. The projecting members 20, 21 are then integrated through the bores of the spacers or supports 44, 45 and the three filter elements 41, 42, 43 at 26, 27 to the wall of the housing portion 2, forming a fluid-tight seal therebetween, and closing off both sides of the filter sheet cascade to fluid flow. The sides 9, 10 of housing portion 2 can also be bonded to the sides 12, 13 of the housing portion 3 by fusion, such as by ultrasonic welding, at the same time or thereafter, so that the two housing portions 2, 3 are sealed together, preventing fluid leakage to the outside of the filter assembly.

Next, the side caps 30, 31 are bonded across the openings 28, 29 into the housing portions 2, 3 and to the filter sheet cascade and spacer composite edges 32, 33, bonding the filter sheet sides and spacer or supports to the side caps, and completing the fixing of the filter sheet cascade and spacer composite 40 in place in the fluid chamber 4, as well as the seals between the filter sheet cascade and the four side walls of the housing. This can be done using, for example, an adhesive, or a melt of adhesive or resin or other potting composition, or by fusing the end caps. The filter unit is now complete, and ready for use.

The filter unit is operated in line, as follows. The spiked tip is plunged into the stopper of a blood bag, thereby permitting blood to flow from the bag through the inlet port 5 and enter the channel 14 flowing into chamber portion 34. The blood then flows through the filter sheet cascade and spacer composite 40 via filter sheet 41, filter sheet 42, spacer 44, filter sheet 43, and spacer 45, and enters the chamber portion 35, whence it emerges via channel 14 from the housing via port 6.

Line connections can be made at ports 5, 6 in any desired manner. Luer locks also can be used, if desired.

The filter unit 50 of *Figures 4 to 6* has as the filter element a composite 60 of a three-component filter sheet cascade (sheets 41, 42, 43) and two spacer or support sheets 44, 45 in corrugated shingled form, with corrugated folds 51 lying in overlapping fashion. The three filter sheets 41, 42, 43 and spacers or support sheets 44, 45 are arranged exactly as shown in *Figure 3*, with the filter sheet 41 outermost and support sheet 45 innermost in the closed configuration shown in *Figures 4 to 6*. The corrugated shingled composite 60 is heat-sealed at 52 along its four sides (or along three sides, if folded on itself). The thus-enclosed filter sheet composite 60 has an outlet line connection via the tube 53 extending into its open interior space 54, and terminating in a caged tip 55. The only inlet into the interior space 54 is through the filter sheet cascade. This type of filter element is especially useful in a flexible bag-type of filter unit, the bag 56 being shown in dashed lines in *Figures 4 and 5*. The other end of the bag 56 which can be the blood bag itself can have an inlet tube 57, for reception of blood. It is also possible to have a spiked inlet tube 57 open onto the outside of composite 60 in bag 56, in which case it can be heat-sealed to the bag 56. This unit can then be plugged into a blood bag, as in the case of the filter unit of *Figures 1 and 2*,

with filter sheet 41 outermost and spacer or support 45 innermost.

The type of filter element shown in *Figures 4 to 6* is especially useful for transfusion blood filtration, in which case it can be built into a standard blood bag, but it can also be attached to any type of blood storage reservoir or receptacle.

The corrugated configuration of this filter sheet cascade provides high surface area, and the shingled arrangement of the corrugations makes it possible to provide a flat pouch without the need for a core support, because the spaces between the shingles act as conduits while at the same time the shingled overlapping structure provides structural support. The support or spacer sheets 44, 45 of the filter cascade are of heat-softenable material, which softens at a lower temperature than any of the three filter sheets composing the cascade, so that the three filter sheets 41, 42, 43 are not affected under the conditions at which the spacers soften, so that the latter can be fused together in a leak-tight heat seal through the filter sheet pores without deleteriously affecting the filter sheets. The heat seal is easily effected by high frequency heat, and all heat seals can be formed simultaneously, including the heat seals with the tubes.

WHAT WE CLAIM IS:—

1. A blood filter cascade comprising in combination, three filter sheets, arranged in downstream flow sequence in order of progressively decreasing porosity,

(a) the first filter sheet comprising coarse open netting of filamentary plastics material having a pore size within the range from about 800 to about 4,000 microns;

(b) the second filter sheet comprising an open mesh fabric of plastics monofilaments, having a pore size within the range from 20 to 53 microns; and

(c) the third filter sheet comprising a non-woven fibrous mat having a pore size within the range from 10 to 30 microns.

2. A blood filter cascade according to claim 1, in which the first filter sheet is an open netting prepared by extruding, casting, or molding plastics and having an integral filamentary structure.

3. A blood filter cascade according to claim 2, in which the plastics material of the first filter sheet is polypropylene, polyethylene, polyester, polyamide, or polycarbonate.

4. A blood filter cascade according to any one of the preceding claims, in which the second filter sheet is a woven square-weave mesh of plastics monofilaments, the filaments being locked in place at their crossing points.

5. A blood filter cascade in accordance with claim 4, in which the monofilaments have a diameter within the range from 20 to 50 microns.

6. A blood filter cascade in accodance with claim 4 or claim 5, in which the monofilaments are of polyester plastics.

7. A blood filter cascade in accordance with any one of claims 4 to 6, in which the monofilaments are heat set to lock them in place.

8. A blood filter cascade according to any one of the preceding claims, in which the third filter sheet is a paper sheet.

9. A blood filter cascade according to any one of claims 1 to 7 in which the third filter sheet is of a fibrous material selected from glass fibres, polyester fibers, polyamide fibers, polyethylene fibers, polypropylene fibers, and polycarbonate fibers.

10. A blood filter cascade according to claim 8 or 9, in which the third filter sheet comprises a layer having a pore diameter larger than 30 microns, and carrying a microporous layer laid down thereon to bring the pore size to within the range from 10 to 30 microns.

11. A blood filter cascade according to any one of the preceding claims, in which the three filter sheets are in close juxtaposition, with the second and third filter sheets separated by a spacer, and all corrugated or convoluted to provide a high surface area to flow.

12. A blood filter cascade according to claim 11, in which the spacer has a pore size at least as large as the first filter sheet, and within the range from 800 to 10,000 microns.

13. A blood filter cascade according to claim 11 or claim 12, in which the spacer has an uneven surface so as to provide drainage and prevent blocking of the second and third filter sheets by the spacer.

14. A disposable blood filter unit comprising a blood filter cascade according to any one of the preceding claims, and a housing having an inlet port and an outlet port for fluid flow into and out from the housing, the blood filter cascade being disposed in the housing across the line of flow between the inlet and outlet ports so that fluid flow through the housing must pass through the filter cascade.

15. A disposable blood filter unit in accordance with claim 14, in which the blood filter cascade is in the form of a corrugated cylinder, one of said ports having a direct fluid flow connection to the interior of the filter cylinder.

16. A disposable blood filter unit in accordance with claim 14 or claim 15, wherein the housing has two portions bonded together.

17. A disposable blood filter unit in accordance with claim 16, in which the

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housing portions are made of plastics with the portions fused together into an integral structure.

18. A disposable blood filter unit in accordance with claim 16 or claim 17, including line connections integral with the housing.

19. A disposable blood filter unit in accordance with claim 16 or claim 17, having a blood filter cascade bonded to at least one housing portion.

20. A disposable blood filter unit in accordance with any one of claims 16 to 19, having the blood filter cascade bonded to at least one housing portion in relation to the outlet port so as to give direct fluid flow for the filtrate between the cascade and the outlet port.

21. A disposable blood filter unit according to claim 14, in which the housing is composed at least of first and second housing portions, defining therebetween a fluid chamber open at two sides, the first and second housing portions having opposed sides, with mating sections abutting and bonded in a fluid-tight seal to each other, and the blood filter cascade extending across the fluid chamber, across the line of fluid flow between the inlet and outlet ports and held at opposed side portions to at least one of the first and second housing portions, and side caps bonded to the first and second housing portions in a fluid-tight seal across the open sides of the fluid chamber and to the sides of the blood filter cascade extending along such open sides, the side caps and the housing portions holding the sides of the blood filter cascade, positioning the blood filter element cascade across the fluid chamber, and sealing all the sides of the blood filter cascade to the housing, so that the fluid flow between the inlet and outlet ports must pass through the blood filter cascade.

22. A disposable blood filter unit in accordance with claim 21, having four sides, two of the sides being defined by the side caps and two of the sides by the first and second housing portions, and the blood filter cascade is formed from four-sided sheets.

23. A disposable blood filter unit in accordance with claim 22, in which the blood filter cascade is in rectangular corrugated sheet form.

24. A disposable blood filter unit in accordance with any one of claims 21 to 23, in which the first and the second housing portions and the inlet and outlet ports therein are arranged so that the inlet and outlet ports are coaxial.

25. A disposable blood filter unit in accordance with any one of claims 21 to 23, in which all of the housing portions are of plastics material.

26. A disposable blood filter unit in accordance with claim 25, in which the plastics material is a thermoplastic resin.

27. A disposable blood filter unit in accordance with claim 26, in which the thermoplastics resin is polypropylene.

28. A disposable blood filter unit in accordance with any one of claims 25 to 27, in which the housing portions are joined together to form an integral structure.

29. A disposable blood filter unit in accordance with any one of claims 21 to 28, in which the blood filter cascade is held at opposed side portions between the mating sections of the first and second housing portions.

30. A disposable blood filter unit in accordance with claim 29, in which the blood filter cascade is joined to the housing portions by fusion thereof through the pores of the blood filter cascade.

31. A disposable blood filter unit in accordance with any one of claims 21 to 30, in which the side caps are joined to the housing portions to form an integral housing.

32. A disposable blood filter unit in accordance with any one of claims 21 to 31, in which each of the housing portions includes at least one projecting portion engaging and supporting opposite sides of the blood filter cascade, and extending with the blood filter cascade across the fluid chamber.

33. A disposable blood filter unit in accordance with any one of claims 21 to 32, in which a first housing portion comprises projecting members holding the opposite side portions of the blood filter cascade against the other housing portion.

34. A disposable blood filter unit in accordance with claim 33, in which the mating sections of each housing portion have abutment members extending towards each other, and abutting endwise, with the first housing portion having the said projecting members extending internally of the abutment members, and engaging the blood filter cascade at the opposite side portions thereof.

35. A disposable blood filter unit in accordance with claim 34, in which the said projecting members also hold the blood filter cascade tightly against an internal wall of the said other housing portion.

36. A blood filter cascade substantially as shown in Figs 1 to 3 or Figs 4 to 6 of the accompanying drawings and described herein with reference thereto.

37. A disposable filter unit substantially as shown in Figs. 1 to 3 or Figs. 4 to 6 of the accompanying drawings and described herein with reference thereto.

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BNSDOCID: <GB_____1440027A__I_>

1 440 027 COMPLETE SPECIFICATION
2 SHEETS *This drawing is a reproduction of the Original on a reduced scale.*
SHEET 1

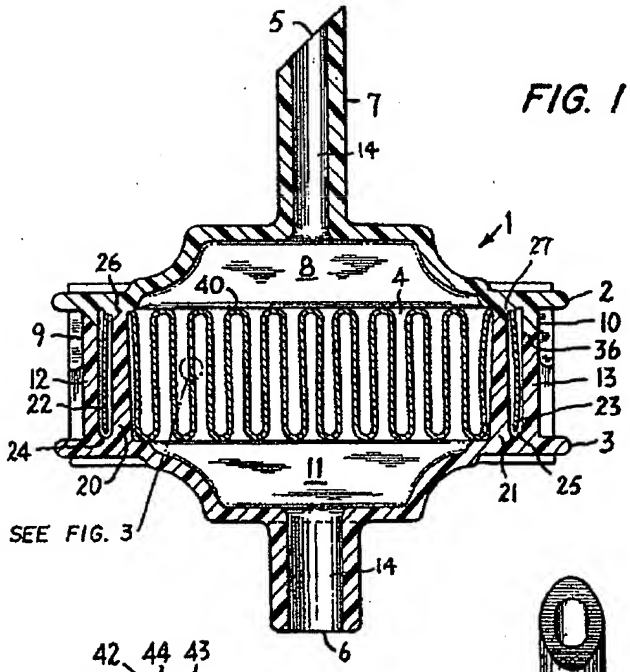


FIG. 1

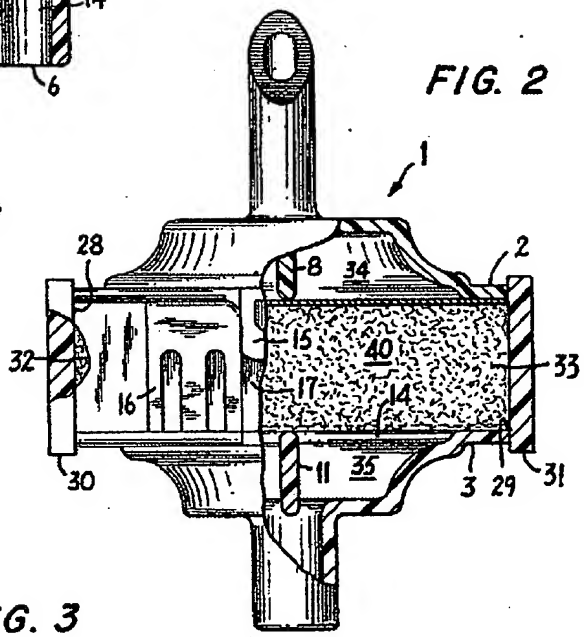


FIG. 2

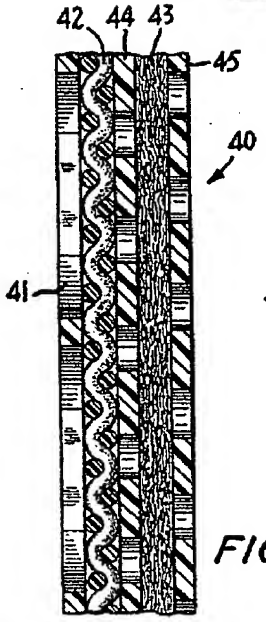


FIG. 3

1 440 027 COMPLETE SPECIFICATION
2 SHEETS *This drawing is a reproduction of the Original on a reduced scale.*
SHEET 2

FIG. 4

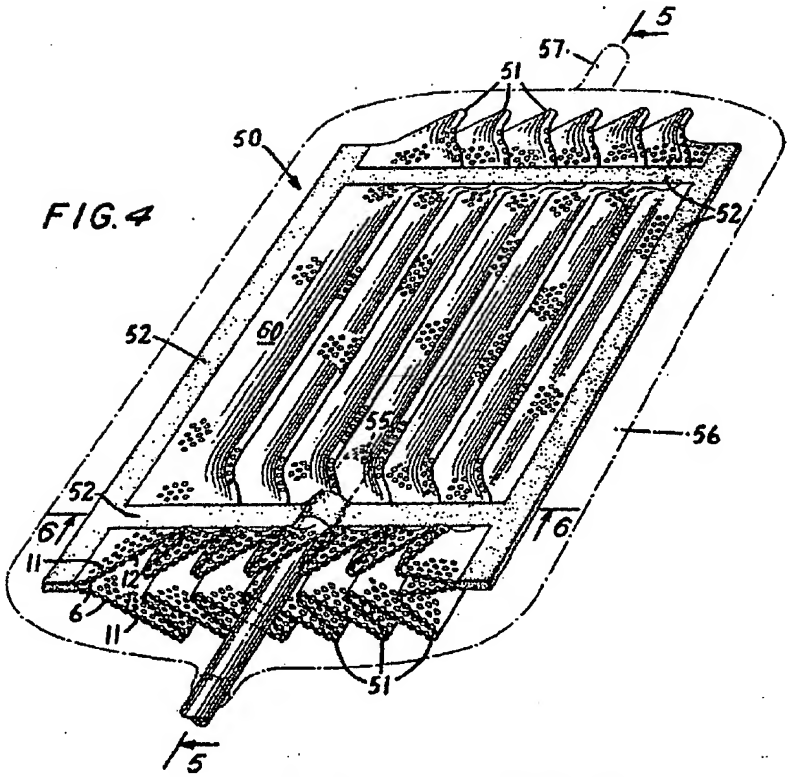


FIG. 5

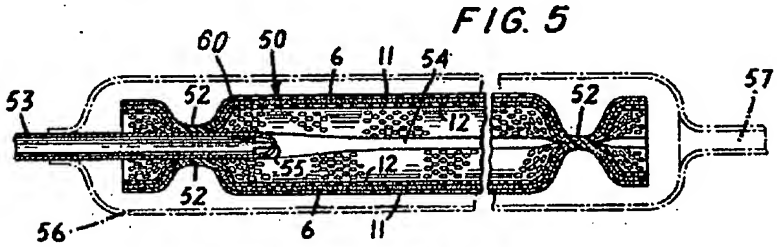
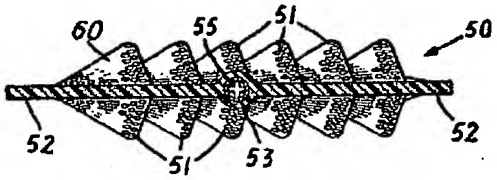


FIG. 6



INSDOCID: <GB_____1440027A__I_>

PATENT COOPERATION TREATY

Translation

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY.

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference H2042-01	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/003835	22.03.2004	24.03.2003

International Patent Classification (IPC) or both national classification and IPC

Applicant
JMS CO. LTD.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/003835

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

PAGE 21/23 * RCVD AT 8/9/2007 1:31:01 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/14 * DNIS:2738300 * CSID:612-455-3801 * DURATION (mm-ss):18-30

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/JP2004/003835

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2-9, 14-16	YES
	Claims	1, 10-13	NO
Inventive step (IS)	Claims	15	YES
	Claims	1-14, 16	NO
Industrial applicability (IA)	Claims	1-16	YES
	Claims		NO

2. Citations and explanations:

Document 1: JP 09-508564 A (Avecor Cardiovascular, Inc.) 2 September 1997
Document 2: JP 2000-517240 A (Sartorius AG) 26 December 2000

Based on the description in document 1 cited in the international search report, the inventions of claims 1 and 10-13 lack novelty. Document 1 (entire text, Figs. 3 and 7) discloses a "sheet-like filter material folded to form pleats that, as a whole, has a planar plate-like outer shape and is installed so as to partition the cavity of the housing into the dome portion side and the bottom portion side" of claims 1 and 10-13.

Based on the descriptions in documents 1 and 2 cited in the international search report, the invention of claim 2 lack an inventive step. The inventions of documents 1 and 2 address the same technical problem of affixing a filtration filter in a housing. This examination finds that it is obvious to persons skilled in the art to adopt the means whereby "a sealing material is bonded to the edge of the filter element attached tightly to the wall of the housing" that is described in document 2 to the invention described in document 1 to solve the common technical problem.

Based on the descriptions in documents 1 and 2 cited in the international search report, the inventions of claims 3-9 lack an inventive step. Optimization of the size of the housing and the shape of the filter are merely matters of design conventionally practiced by persons skilled in the art.

Based on the descriptions in documents 1 and 2 cited in the international search report, the inventions of claims 14 and 16 lack an inventive step. This examination finds that it is obvious to persons skilled in the art to adopt the means whereby "a sealing material is adhered to the housing wall by centrifugal force such that on one surface it is bound to half the housing and on the other surface the housing wall is bound to the edge of the filter element" that is described in document 2 to the invention described in document 1 to solve the common technical problem.

None of the documents cited in the international search report discloses the invention of claim 15, and therefore this invention is novel. More particularly, none of the documents discloses "retaining ribs in a vertical orientation positioned on the inner wall of the filter retention member and located opposite the edge of each pleat of the filter.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/JP2004/003835

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The invention of claim 16 refers to the "aforementioned resin packing and curing process step according to claim 14 or 15," but a "resin packing and curing process step" is not described in claim 15; claim 11, cited in claim 15; or claim 1, cited in claim 11. Therefore, the meaning of the "resin packing and curing process step" cannot be understood.

PAGE 23/23 * RCVD AT 8/9/2007 1:31:01 PM [Eastern Daylight Time] * SVR:USPTO-EFXRF-1/14 * DNIS:2738300 * CSID:612-455-3801 * DURATION (mm-ss):18-30